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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,968	05/04/2005	Vincent Goffin	255563US0PCT	1164

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EXAMINER	
SAOUD, CHRISTINE J	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
11/06/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/500,968	GOFFIN ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *10-12 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 13-19 and 21-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed 27 July 2009 has been received an entered. Claims 21-22 have been added. Claims 1-22 are currently pending. Claims 10-12 and 20 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 06 December 2007.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in ths action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 27 July 2009 have been fully considered, but are not found persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 and 13-19 remain rejected and newly added claims 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goffin et al. (J. Biol. Chem. 271(28): 16573-16579, 1996) in view of Bernichtein et al. (Endocrine Society 82nd Annual Meeting, Toronto, June 21-24, 2000, Abstract 613) for the reasons of record as applied to claims 1-9 and 13-19 in the previous Office action.

Goffin et al. teach human prolactin analogs wherein position 129 is mutated from glycine to arginine. This amino acid substitution results in a prolactin molecule which has antagonistic properties. The modification of this amino acid results in antagonism of binding to the receptor at site 2. Molecules in this protein family (growth hormone, prolactin and placental lactogen) bind to their receptors via 2 distinct binding sites. Goffin et al. also teach recombinant methods of making these mutations, including nucleic acids, vectors and host cells. Goffin et al. do not teach modification of the N-terminus of prolactin.

Bernichtein et al. teach N-terminal deletions of human prolactin wherein the N-terminal 1-9 amino acids were deleted in combination with a substitution of the cysteine residue at position 11 with methionine as well as a deletion of amino acids 1-14.

Bernichtein et al. found that deletion of residues 10-14 impairs binding to both sites 1 and 2 with the prolactin receptor. Bernchtein et al. suggest that antagonistic properties of site 2 analogs could be enhanced if paired with a deletion of residues 10-14, which increases site 1 affinity.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the mutations of Goffin et al. and Bernichtein et al. to arrive at a prolactin molecule which has a mutation at position 129 and an N-terminal truncation of the first 9 amino acids in order to create a prolactin antagonist which has an increased affinity for site 1. One would be motivated to combine these two modification based on the teachings of Bernichtein et al. Additionally, the references teach all the necessary methods for making the prolactin antagonists, including nucleic acids, vectors and host cells as well as a reasonable expectation of success in making such molecules based on the suggestion of Bernichtein et al. Therefore, the invention as a whole would have been prima facie obvious at the time it was made, absent evidence to the contrary.

Response to Arguments

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., pure antagonism) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues at page 9 of the response that the G129R prolactin analog of Goffin has a residual agonist activity which is not shown by the analogs of the claimed invention. Applicant further argues that one of ordinary skill in the art following the suggestions of Bernichtein would have first logically tested the molecules for their affinity for the prolactin receptor and for their antagonistic properties and in testing the affinity of the molecules, the ordinary artisan would have found that the N-terminal deletion does not increase the affinity of site 2 analogs. Applicant asserts that serious doubt would have resulted that an improvement of the antagonistic properties was to be expected, and the ordinary artisan would have discarded the suggestion of Bernichtein.

Applicant's argument has been fully considered, but is not found persuasive. First, in order to test the molecules suggested by Bernichtein, one would have had to make the molecules. It would appear that Applicant is not questioning the suggestion in the art to indeed produce a prolactin variant which has a mutation at position 129 as taught by Goffin and includes a truncation of the N-terminus as taught by Bernichtein. The art clearly directs one of ordinary skill in the art to do exactly this in order to "enhance the antagonistic properties of site 2 analogs by increasing site 1 affinity" as taught in Bernichtein. Applicant is asserting that a reasonable expectation of success is not provided by the prior art because an increase in binding affinity was not obtained as evidenced by the binding assay of the instant application. Applicant's arguments have been fully considered, but are not found persuasive. The prior art asserts that enhanced antagonist properties will be obtained for the site 2 analogs by increasing site 1 affinity - the prior art does not allege that binding affinity in general for the entire

molecule will be obtained. Therefore, the expectation from the prior art is that one would realize an enhanced antagonistic property of the prolactin variant by combining the site 1 mutations with the site 2 mutation with the end result being a prolactin receptor antagonist. This is indeed what is obtained when combining the mutation of Goffin with the mutations of Bernichtein, absent evidence to the contrary.

Applicant argues at page 10 of the response that if the teachings of Bernichtein were followed, one of ordinary skill in the art would have "considered that the combination of N-terminally deletions with site 2 mutations was of no use, and would have discarded this approach". Applicant's arguments have been fully considered but are not found persuasive. One of ordinary skill in the art would expect to obtain a prolactin receptor antagonist with enhanced properties, which is exactly what was obtained, absent evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christine J Saoud/

Primary Examiner, Art Unit 1647